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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,978	04/25/2001	Susana Salceda	DEX-0172	3638

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LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,978	SALCEDA ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,21-28 and 35-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,21-28 and 35-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 4/26/06 in response to the Office Action of 12/28/05 are acknowledged and have been entered.

Claims 14, 21-28, and 35-49 were pending.

Claims 14, 21-28, and 35-49 are currently under examination.

The text of those sections of Title 35 U.S.C. code not included in this Office Action can be found in a prior Office Action.

Response to Arguments

35 USC § 101 (Utility Rejection) &

35 USC, 112.1 (Enablement and Written Description Rejections)

Claims 14, 21-28, and 35-49 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial utility or a well established utility for the reasons of the Office Action of 12/28/05 and the reasons set-forth below. Further, claims 14, 21-28, and 35-49 remain rejected under 35 U.S.C. 112, first paragraph, because the claimed invention is not supported by either a substantial utility or a well established utility for the reasons of the Office Action of 12/28/05 and the reasons set-forth below. Further, claims 14, 21-28, and 35-49 remain rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, for the reasons of the Office Action of 12/28/05 and the reasons set-forth below.

The Office Action of 12/28/05 contains the following text:

The claims are drawn to isolated antibodies or antibody fragments that bind specifically to a protein encoded by polynucleotide SEQ ID NO:1 or to fragments of a protein encoded by SEQ ID NO:1 and a method for binding said antibodies to said protein or to fragments of said protein.

The Response filed on 11/22/05 has been carefully considered but is deemed not to be persuasive. The Response cites MPEP 2107.02 and states that utility of the claimed invention is set forth in detail in the specification (page 10 of Response). Applicant further cites Raytheon v. Roper and MPEP 2107.02 (page 10 of Response). Applicant further states the Office must establish that it is more likely than not that one of ordinary skill in the art would doubt (i.e. "question") the truth of the statement of utility in order to overcome the "presumption of truth that an assertion of utility by the applicant enjoys" (page 10 of Response). Applicants further state that "no such evidence that the statement of asserted utility for the instant claimed invention would be considered false by the skilled has been provided by the Examiner in the instant case" (page 10 of Response). In contrast, Applicants argue that confirming evidence by Tringler and Salceda (submitted in the response filed 5/3/05) demonstrate that the claimed invention is useful in the manner taught in the originally filed application (pages 10-11 of Response).

A Declaration from Dr. Susana Salceda accompanied the Response filed on 11/22/05. The Response indicates that the Declaration "makes clear that any experimentation necessary to make and use the invention as claimed was routine to the

skilled artisan when coupled with the information taught in the specification" (pages 11-12 of Response). The Response, citing the MPEP and case law, further states that information well known in the art does not need to be described in detail in the specification (page 14 of Response). The Declaration suggests that one of skill in the art would "know that the open reading frame in the forward direction of SEQ ID NO:1 would be in a frame encoding for a Methionine near the 5' end, encode many amino acids and terminate with a stop codon. Thus, any open reading frame of SEQ ID NO:1 with lots of stop codons can be ruled out since we know to look for a long open reading frame sequence beginning with an M and ending with a stop codon in accordance with the information taught in the patent application about SEQ ID NO:1" (page 3 of Declaration). The Declaration further suggests one of skill in the art had many tools available before the time of filing that would help identify potential open reading frames from a given sequence (page 3 of Declaration). Further, Dr. Salceda provided examples of computer-generated open reading frames using instant SEQ ID NO:1 (pages 4-5 of Declaration and attached examples). The Response states that these examples indicate that there was only one possible open reading frame for a full-length protein (page 13 of Response and frame 2 of Figure 2 from Declaration). The Response and Dr. Salceda further argue that SEQ ID NO:1 was not a "starting point(s) for further research and investigation into potential practical uses", rather "the nucleotide sequence of SEQ ID NO:1 and the characteristics disclosed in the patent application about SEQ ID NO:1 were adequate to routinely and unambiguously obtain the protein sequence and then generate antibodies or antibody fragments thereto" (pages 5-6 of

Declaration and page 14 of Response). It is further argued that the uses for the protein encoded by SEQ ID NO:1, for detecting, diagnosing, and treating cancer, are explicitly described in the specification (page 6 of Declaration and page 14 of Response, in particular).

The amendments to the claims and the arguments found in the Response and the Declaration filed on 11/22/05 have been carefully considered but are deemed not to be persuasive. As stated in the previous Office Action, the specification did not teach the protein sequence or the open reading frame of SEQ ID NO:1. Thus, the specification did not provide enough information to indicate for which protein the claimed antibody is specific. Therefore, the specification clearly does not describe a utility for an antibody with unknown specificity. Thus, one of ordinary skill in the art would doubt any truth to a stated utility. Further, as indicated above, there were routinely-used methods at the time of filing that would have enabled one of skill in the art to identify *potential* open reading frames from an mRNA sequence. However, as indicated in the figures provided with the Declaration, Applicants would identify multiple open reading frames using the tools described above with SEQ ID NO:1. One of skill in the art would have no reason to assume that the open reading frame would "encode many amino acids" and that the largest open reading frame identified by a computer program would be *the* protein encoded by SEQ ID NO:1. From the information provided in the specification, there is no reason to believe that the protein of SEQ ID NO:1 would not be encoded by other smaller open reading frames diagramed in the Declaration's figures. Therefore, since the specification does not identify "a protein encoded by

polynucleotide SEQ ID NO:1", it cannot be determined to what the claimed antibody or antibody fragment will bind. Further, although Tringler and Salceda demonstrate utility of an antibody against "a" protein of SEQ ID NO:1, the specification did not teach "the" protein of SEQ ID NO:1. Therefore, utility of an antibody specific for a protein that the specification did not adequately describe is irrelevant. Essentially, the specification does not describe what the protein *is*. Thus, there is no utility for the claimed antibodies, antibody fragments, or methods of using said antibodies or said antibody fragments.

Claims 14, 21-28, 35-37 remain rejected and new claims 38-49 are rejected under 35 U.S.C. 112, first paragraph, because the claimed invention is not supported by either a substantial utility or a well established utility for the reasons of the previous Office Actions and for the reasons set-forth above.

Claims 14, 21-28, 35-37 remain rejected and new claims 38-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of the previous Office Actions and for the reasons set-forth above.

The Response filed on 11/22/05 has been carefully considered but is deemed not to be persuasive. It is noted that claims 14 and 28 have been amended to remove references to polynucleotide sequences other than SEQ ID NO:1. Further, the Response states that antibodies and their uses were described in detail and were claimed in the original specification (page 15 of Response). Further, Applicant states native protein and method for detection thereof are described in the original application

(pages 15-16 of Response). Further, Applicants cites passages from the MPEP and case law, which are asserted to suggest that Applicant was in possession of the claimed invention at the time of filing. Applicant states "the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined in the claims. MPEP 2163 at pate 2100-166; In re Wertheim, 541 F.2d 257 at 263, 191 USPQ 90 at 97 (CCPA 1976). Moreover, if the skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description is met. Also see Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Possession may be shown in a variety (of) ways including describing distinguishing identifying characteristics to show that applicants (were) in possession of the claimed invention. See MPEP 2163. Precisely how close [to the claimed invention] the description must come to comply with 112 must be left to case-by-case-development. In re Wertheim, 541 F.2d at 262, 191 USPQ at 96 (inquiry is primarily factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure). Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure and/or chemical properties, functional characteristics alone or coupled with a known or

disclosed correlation between structure and function, and the method of making the claimed invention. Disclose of any combination of such identifying characteristics that distinguish the claimed invention from other materials would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See MEPE 2163 at page 2100-73 and Reagents of the University of California B. Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406 (Fed. Cir. 1997). Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art. In most technologies which are mature, and wherein the knowledge and level of skill in the art is high, a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention. See, e.g. In re Hayes Microcomputer Products, Inc. Patent Litigation, 982 F .2d 1527, 1534-1535, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992)." (Pages 16-17 of Response).

Further, the Response argues that Dr. Susana Salceda's Declaration indicates Applicant had a written description of the claimed invention. Specifically, Applicant argues that Dr. Salceda's Declaration indicates that sufficient distinguishing characteristics were taught in the specification so that using standard tools available to those skilled in the art as of the filing date of the instant application that every nuance of the protein sequence and/or the open reading frame of SEQ ID NO:1 could be routinely determined (pages 18-20 of Response). As described above, Dr. Salceda declared that there was only one possible open reading frame for the full-length protein encoded by SEQ ID NO:1 (page 13 of Response and frame 2 of Figure 2 from Declaration).

The amendments to the claims and the arguments found in the Response and the Declaration filed on 11/22/05 have been carefully considered but are deemed not to be persuasive. As stated above and in the previous Office Action, the specification did not teach *the* protein sequence or the open reading frame of SEQ ID NO:1. Thus, the specification did not provide enough information to indicate for which protein the claimed antibody is specific. As indicated above, there were routinely-used methods at the time of filing that would have enabled one of skill in the art to identify *potential* open reading frames from an mRNA sequence. However, as indicated in the figures provided with the Declaration, Applicants would identify multiple open reading frames using the tools described above with SEQ ID NO:1. One of skill in the art would have no reason to assume that the open reading frame would "encode many amino acids" and that the largest open reading frame identified by a computer program would be *the* protein encoded by SEQ ID NO:1. From the information provided in the specification, there is no reason to believe that the protein of SEQ ID NO:1 would not be encoded by other smaller open reading frames diagramed in the Declaration's figures. Therefore, since the specification does not identify "a protein encoded by polynucleotide SEQ ID NO:1", it cannot be determined to *what* the claimed antibody or antibody fragment will bind. Therefore, it is determined that Applicant was not in possession of the claimed antibody or in possession of the protein to which the claimed antibody binds. Even though generating antibodies is rather routine in the art, it is not possible to make an antibody specific for an unknown protein. Essentially, the specification does not describe what

the protein *is*. Thus, there is no written description for the claimed antibodies, antibody fragments, or methods of using said antibodies or said antibody fragments.

In response to the Office Action of 12/28/05, Applicant argues that in addition to the methods of identifying open reading frames by scanning a polynucleotide sequence for ATG "start sites", also known as of the filing date was that the sequences flanking functional initiator codons in eukaryotic mRNA sequences is a nonrandom sequence, referred to as the Kozak consensus sequence. Applicant further argues that the first ATG start codon in frame 2 of SEQ ID NO:1 and the flanking sequence, CCAGCCATGC, meet the requirements for an initiator codon as identified by the Kozak eukaryotic sequence. Applicant further states that said ATG is the same ATG identified in Dr. Salceda's declaration as the start of the open reading frame for the protein encoded by SEQ ID NO:1. Based on these arguments, Applicant concludes that the nucleotide sequence of SEQ ID NO:1, coupled to the teachings in the specification regarding the sequence being based on an mRNA molecule and having a set 5' to 3' orientation, the methods available as of the filing date of the application for what was known in the art for identifying potential open reading fames (ATG start sites), and what was known in the art regarding translation initiation of eukaryotic mRNA sequences (Kozak sequences), that Applicant was in possession of the protein encoded by SEQ ID NO:1 and provides the required enablement for one of skill in the art at the time of filing to make and use the protein encoded by SEQ ID NO:1 and antibodies thereto. Applicant further cites case law and MPEP 2163 and MPEP 2164.01; information which is well known in the art need not be described in detail in the specification "See, e.g.

Hybritech, Inc. v. Monoclonal Antibodies, Inc. 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)". Applicant concludes that detailed teachings in the specification of the methods available for identifying the open reading frame, the initiator codon based on the Kozak consensus sequence, and the 5' proximal ATG are not required to meet the written description and enablement requirements of 35 U.S.C. 112, first paragraph.

The arguments found in the response of 4/26/06 have been carefully considered but are deemed not to be persuasive. In regards to Applicant's argument that protein sequences and/or open reading frames were routinely obtained by those of skill in the art at the time of filing based upon identifying ATG start sequences and Kozak consensus sequences, this guidance and essential information was not provided in the originally filed application. Further, Kozak (The Journal of Cell Biology, 1991, 115(4):887-903) teaches that Kozak consensus sequences are not found at the start of *every* open reading frame (see right column of page 887 and left column of page 888, in particular); rather, they are the most frequently occurring sequences flanking functional initiator codons of open reading frames. Further, SEQ ID NO:1 contains numerous ATG "start sites" and the originally filed application gives no guidance for identifying which of said ATG "start sites" marks the 5' end of an open reading frame. Further, Kozak sequences are not specifically *defined* sequences; rather, Kozak sequences are "non-random sequences" comprised of different nucleotides and are described by a "likelihood" of the order of said nucleotides within a sequence. Since Kozak sequences are not defined by one *specific* sequence, it is unclear whether the asserted Kozak sequence near position 62 is the only bona fide Kozak sequence in SEQ ID NO:1, a

region encoding the middle of a protein encoded by SEQ ID NO:1, or a region outside of an open reading frame of SEQ ID NO:1. Further, in the Response of 4/26/06, Applicant states that the ATG codon beginning at position 62 of SEQ ID NO:1 and the flanking sequence, CCAGCCCATGC, meets the requirements for an initiator codon as identified by the Kozak eukaryotic sequence and said ATG is the same ATG identified by Dr. Salceda in her declaration as the start of the open reading frame for the protein encoded by SEQ ID NO:1. However, it is noted that Dr. Salceda declared that the sequence of the protein encoded by SEQ ID NO:1 was based on said sequence being the longest potential open reading frame rather than being based on said sequence being flanked by a Kozak sequence. Therefore, it is clear from the record that identification of start sites based on Kozak sequences is not as routine as Applicant asserts.

In regards to Applicant's argument that the test of enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosure coupled with information known in the art without undue experimentation, without explicitly disclosing the claimed invention one would not know how to make or use said claimed invention. The specification provides no guidance regarding how one could identify an open reading frame in SEQ ID NO:1. Without identifying said open reading frame and without identifying the protein encoded by said open reading frame, one would not know what the antibody recited in the claimed invention is. Therefore, one of skill in the art would not know how to produce the antibody recited in the claims or how to use information known in the art to make or perform any method with said antibody.

Further, the written description does not provide a description of the genus of antibodies and antibody fragments that bind to an undisclosed protein encoded by SEQ ID NO:1 since one would not know what the genus of antibodies that bind to an undisclosed protein would comprise. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. The specification does not disclose the protein encoded by SEQ ID NO:1. The specification does not provide any examples of the genus of antibodies that bind to the undisclosed protein expressed by the nucleotide sequences SEQ ID NO:1. Further, the specification does not provide a description of structural features that are common to said genus. Further, as stated in the Office Action of 1/3/06: "Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016".

In regards to Applicant's citation of MPEP 2163 and Hybritech, Inc. v. Monoclonal Antibodies, Inc. 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986) ("information which is well known in the art need not be described in detail in the specification"), it is noted that the protein of SEQ ID NO:1, and the antibody to which it binds, are *not* well-known in the art. Further, although methods of generating antibodies to disclosed proteins are well-established procedures, methods of generating antibodies to undisclosed proteins are not well-established procedures. Essentially, the specification does not disclose exactly what the protein encoded by SEQ ID NO:1 is or

provide any *guidance* that would lead one to conclude what the protein encoded by SEQ ID NO:1 is. Thus, there is no written description for the claimed antibodies or antibody fragments. Without clearly identifying what the antibodies or antibody fragments are, one would not know what to use in any kind of method drawn to said antibodies or antibody fragments.

Summary

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a). A shortened statutory period for response to this Final Action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this Final Action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. '1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than six months from the date of this Final Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

SEA